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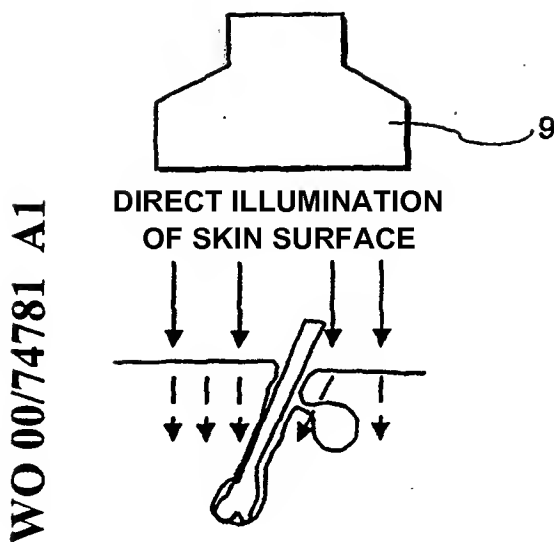
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(54) Title: COSMETIC DEPILATION KIT WITH PHOTSENSITIZER



(57) Abstract: A marker substance includes a photosensitive toxic material to tag **subcutaneous** hair growth cells of a target zone of skin. Illumination apparatus is used to illuminate the skin in the target zone with light of a wavelength selected to effect preferential interaction with the hair growth cells tagged with the marker **substance, resulting in a toxic effect inhibiting the hair growth capability of the tagged illuminated cells; wherein.** In the kit the marker substance may be **provided** in a form comprising discrete portions of the **photosensitive toxic material and** a carrier material, the portions to be mixed prior to **application** to the target zone. Additionally or alternatively, the illumination apparatus includes an applicator configured to deliver non-laser light and/or configured to be placed against the target zone skin to deliver the illumination to the tagged hair growth cells.

**COSMETIC DEPILATION KIT WITH PHOTSENSITIZER**

The present invention relates to a cosmetic depilation kit.

Laser hair removal is currently an effective and long term method for effecting cosmetic hair removal. An exemplary laser depilation technique is disclosed in EP-A-0732895. In such techniques, high intensity laser energy is directed towards the skin selectively heating hair surrounding the follicle leading to damage of the hair growth mechanism. If sufficient damage is induced, the hair follicle **is** effectively destroyed and the **hair** will not regrow. This technique has disadvantages, one such being that scarring and pigmentary changes can occur. This is particularly the case where the individual being treated has dark skin and/or light hair. Such techniques are also relatively slow, with the target zone needing to be covered by repeated laser pulses.

**US-A-5669916** discloses a technique in which a hair is first plucked from a follicle before a photosensitive toxic material is directed along the path of the removed hair to the follicle. The toxic material is then activated by irradiation using laser.

An improved technique has now been devised.

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According to a first aspect, the present invention provides a cosmetic kit for use in inhibiting hair growth, the kit comprising:

- 5           a) a marker substance including a photosensitive toxic material to tag subcutaneous hair growth cells of a target zone of skin; and,
- 10           b) illumination apparatus for illuminating the skin in the target zone, with light of a wavelength selected to effect, preferential interaction with the hair growth cells tagged with the marker substance, resulting in a toxic effect inhibiting the hair growth capability of the
- 15           tagged illuminated cells; wherein:
- (i) the marker substance is provided in a form comprising discrete portions of the photosensitive toxic material and a carrier
- 20           material, the portions to be mixed prior to application to the target zone; and or,
- (ii) the illumination apparatus includes an applicator configured to deliver non-laser
- 25           light and/or configured to be placed against the target zone skin to deliver the illumination to the tagged hair growth cells.

30           The photosensitive toxic material is a material whose toxicity increases substantially upon exposure

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illumination of predetermined wavelength at sufficient energy delivered. One such material is ALA (aminolevulinic acid); this and other materials are known in the art and described, for example in US-A-5669916.

5

The carrier material is beneficially a material easily absorbed into the skin and preferably comprises a moisturiser or absorbent emollient carrying the photosensitive toxic material in dissolved form or otherwise. It is important to maintain the carrier and the photosensitive toxic material separate until shortly prior to use in order to inhibit any adverse interaction between the materials prior to application to the skin of the target zone.

15

The portions of the photosensitive toxic material and the carrier material are dosed in a predetermined ratio. In one embodiment the proportion would be approximately 25% photosensitive toxic material to approximately 75% carrier material.

20

The kit beneficially includes a dispenser or a container-dispenser for dispensing the marker substance.

25

A container for the carrier material and or the photosensitive toxic material preferably affords light shielding of the photosensitive toxic material.

30

Mixing means is beneficially provided for mixing the photosensitive toxic material and the carrier material. The mixing means preferably permits mixing of the

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photosensitive toxic material and the carrier material at a zone substantially sealed from the user.

Beneficially a container for the photosensitive toxic material and the carrier material comprises respective sealed zones containing the photosensitive toxic material and the carrier material respectively, the zones being configured to be selectively breached or ruptured permitting mixing of the materials. A mixing zone may be provided adjacent the breachable sealed zones, the mixing zone preferably communicating with a dispensing outlet.

The illumination apparatus preferably includes window means arranged to overlay the target zone skin, the illumination being directed via the window means.

In one embodiment, the illumination apparatus includes an illumination applicator having a flexible structure arranged to conform to the target zone skin body part.

20 .

The illumination apparatus preferably includes:

an illumination applicator structure arranged to deliver illumination over a predetermined area;

25

b) a waveguide to connect with the illumination applicator; and,

c) a light source to direct light along the waveguide.

30

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The illumination apparatus beneficially includes an illumination applicator structure having internal light reflecting walls and an associated light transmissive zone means through which reflected light is permitted to pass.

5 This may be achieved, for example, where the applicator structure comprises one or more lengths of fibreoptic (preferably the applicator structure comprises a plurality of lengths of fibre optic, the lengths being arranged to deliver light at different zones of the applicator

10 structure).

The marker substance is desirably preferentially absorbed by, or tagged to, hair growth cells in the target zone. The excess proportion of the applied marker substance not

15 absorbed by the hair growth cells is preferably metabolised and removed from the tissue by the normal action of the body. The technique according to the invention has been found to be effective even without the prior mechanical/physical depilation suggested in US-A-

20 **5669916**. Indeed such a step is discouraged due to the unnecessary trauma and pain it entails.

The hair growth cells targeted for tagging are preferably so called 'stem' cells in the 'bulge' area of the follicle

25 (adjacent the sebaceous gland). By effectively destroying or disabling the 'stem' cells once the hair has completed a growth cycle, a new hair cycle will be inhibited from starting, thereby preventing the follicle from functioning properly. The marker substance is therefore selected to

30 preferentially tag 'stem' cells.

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The marker substance is preferably topically applied to the skin at the target zone. The marker substance penetrates into the skin to preferentially tag the target cells (typically by being preferentially absorbed). The  
5 marker substance preferably comprises a photo therapy drug such as for example 5-Aminolaevolinic Acid (5-ALA). Desirably the drug is provided in a topically administrable form such as a cream or the like.

10 The interaction of the illuminating light with the marking substance preferably results in the desired hair growth inhibition. The interaction may be photochemical and/or photo-thermal in nature. For photochemical interaction, light of a predetermined wavelength induces a chemical  
15 reaction between the marker substance and the tagged cells resulting in destruction of, or disabling of, the tagged cells. For photo-thermal interaction, the incident light causes a temperature rise in the tagged cells to a degree sufficient to destroy or disable the tagged cell.

20 The wavelength of the illuminating light is preferably selected such that it is absorbed by the marker substance (or-the tagged cell). The wavelength of the illuminating light is preferably substantially matched to the optical  
25 absorption characteristics of the marker substance.

The illuminating light is preferably substantially in the range 500nm-100.0nm wavelength. The light is preferably concentrated within a relatively narrow bandwidth within  
30 the range. This may be achieved by filtering of the light or use of light emitting apparatus arranged to emit a

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discrete wavelength (or band of wavelengths). For example where 5-ALA is used as the marker substance to tag the cells it is preferred that the illuminating light includes on or more wavelengths substantially in the range 600nm-  
5 650nm.

The illuminating light may, for example, be laser (including semiconductor laser), white light (preferably filtered), or LED light.

10 The intensity of the light is determined by the quantity of light required to produce the necessary interaction with the tagged cells. Generally however the intensity required will be substantially lower than the intensity  
15 required for prior art laser depilation techniques. This enables the technique to be more suitable for unsupervised 'Home' use.

The light may be pulsed or applied as continuous wave. The  
20 light typically floods the target zone, which target zone is typically of an area in the range  $0.5\text{cm}^2$ - $10\text{cm}^2$ , more preferably  $1\text{cm}^2$ - $5\text{cm}^2$ . The energy applied per pulse to the target zone is preferably substantially in the range 40J or less (more preferably 25J or less).

25 The possibility of using lower intensity and non-laser light also enables a greater area target zone to be simultaneously illuminated, with reduced risk of skin burn. The technique is therefore safer and quicker.

30



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The invention will now be further described, in a specific embodiment, by way of example only and with reference to the accompanying drawings in which:

5       Figure 1 is a schematic representation of a mammalian hair follicle;

          Figure 2 is a schematic representation, similar to Figure 1, showing a first stage in application of the depilation  
10       technique;

          Figure 3 is a schematic representation similar to Figures 1 and 2, showing a subsequent stage in the technique;

15       Figures 4 and 5 are schematic plan and side views respectively of a container-dispenser for the marker substance according to the invention;

          Figures 6 and 7 show alternative general embodiments of  
20       illumination apparatus for inclusion \_in a kit according to the invention;

          Figure 8 is a schematic view of a laser diode illumination  
25       apparatus for inclusion in a kit according to the invention;

          Figure 9 is a schematic view of LED illumination apparatus for inclusion in a kit according to the invention;

30       Figure 10 is a schematic view of .'white light' illumination apparatus for inclusion in a kit according to

the invention;

Figure 11 is a schematic view of alternative 'white light' illumination apparatus for inclusion in a kit according to the invention;

Figure 12 is a schematic view of a pad or patch applicator structure illumination apparatus for inclusion in a kit according to the invention;

Figure 13 is a perspective view of the applicator pad or patch of figure 12;

Figure 14 is a sectional view of the fibreoptic used in the pad or patch of figures 12 and 13; and

Figure 15 is a schematic longitudinal section of the fibreoptic of figure 14.

Referring to the drawings and initially to Figure 1, there is shown human hair follicle supporting a hair shaft 1 growing through the epidermis 2 and dermis 3 of mammalian skin tissue. 'Stem' cells 7 are present in the 'bulge' region 4 adjacent the sebaceous gland 5. Stem cells have a relatively high turnover/life cycle and are responsible for instituting cyclical growth of the hair from the follicle.

In accordance with the invention, a drug formulation including 5-Aminolaevolinic Acid (5-ALA) is provided in a form for topical administration to the outer surface of

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the skin 6. The drug 5-ALA is selected because it is selectively absorbed and retained in stem cells 7 when penetrating into the epidermal layer 3 (via epidermis 2) thereby effectively tagging the stem cells. Concentrations of the drug not absorbed in the stem cells 7 are metabolised and removed from the tissue by the normal-action of the body.

After a predetermining period of time to allow the excess "marker" drug to be removed from the target zone tissue (other than from the "tag" stem cells 7), the target zone of the skin is directly illuminated from externally of the body by means of an illumination device 9 which supplies light of a preselected wavelength matched to a preselected characteristic absorption wavelength of the marker drug (now tagging stem cells 7).

The intensity of the light supplied, and duration of supply of the light, is controlled such that either photochemical or photo-thermal interaction (or both) of the light with the tagged stem cells 7 causes disabling or destruction of the relevant stem cell 7 without disabling or destroying, substantially, the surrounding tissue material. This results in the tagged and disabled stem cell being inhibited from acting further to produce hair from the relevant follicle.

The technique, by selectively marking/tagging and destroying stem cells preferentially (and the associated matching of the wavelength of the illuminating light) enables relatively low intensity light to be used, which

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may flood the target zone of the skin enabling a relatively large area of hair covered skin to be treated simultaneously. Typically, the light from the illumination device 9 is pulsed to enable thermal relaxation of the skin to occur between consecutive pulses. Typically, the energy supplied to the skin surface by the illuminating device 9 does not exceed 25J, before significant thermal relaxation of the skin is permitted.

10

The illuminating device may comprise laser, semiconductor laser, white light illumination device (typically with a filter) or an LED device. The wavelength band width emitted where 5-ALA is used as the marker is preferably substantially within the range 600nm - 650nm (which may be achieved by filtering if required).

The low intensity nature of the light required to effect depilation using the technique according to the invention, enables the technique to be relatively safe when compared to prior art laser hair removal techniques. The drug formulation and illumination device may therefore be sold as a consumer kit for "home" use.

Referring to figures 4 to 15 a "home use" kit for cosmetic depilation would typically comprise a power supply and lighting apparatus 10, 11 (see figures 6 and 7) for direct connection to mains power supply. The apparatus 10, 11 either includes flexible electric connection to a light source 12 for application of illuminating radiation to the skin or, a "fixed" light source 13 and fibreoptic

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connection 14 to an applicator 16.

5 The other essential element of the kit is the market substance typically provided in a container 20 (see figures 4 and 5) which comprises a heat sealed plastics container/dispenser 20 having sealed chambers 21, 22, 23.

10 Chamber 21 contains the ALA material and chamber 23 carries the moisturiser/emollient carrier cream. A manual pinch pressure causes seals 24, 25 to be ruptured and the respective materials to be urged from chambers 21, 23 into mixing chamber 22 where they become thoroughly, and intimately, mixed. A cap 26 is subsequently broken from the end of nozzle 27 permitting the ALA and carrier  
15 mixture to be squeezed out of the container dispenser 20 under manual pressure.

The container dispenser 20 ensures that the correct proportions of ALA drug and carrier are mixed, and that  
20 mixing may be delayed until the point. of application.

Following application of the mixture topically to the target zone of skin, and subsequently waiting the required length of time to permit the concentration of ALA in the  
25 non-target tissue to be reduced to the required low level, the illumination apparatus is applied to the skin and switched on.

Various forms of illuminating apparatus may be used. The  
30 apparatus 110 in figure 8 includes a laser diode light source 125 contained within a protective casing 126 and

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including focussing optics 127 arranged to ensure the light is directed through a protective window 128. Typically the window 128 is held against the skin of the target zone to ensure correct delivery of the illuminating light to the target zone.

In the- embodiment shown in figure 9 a 2D array of LEDs (light emitting diodes) 225 is utilised. Focussing optics 227 ensure the light is directed through the protective window 228 in a similar manner to the arrangement of figure 8.

In the apparatus shown in figure 10, an electric filament "white light" source is used. The source 325 is surrounded by a protective housing 326 including a shaped reflective surface 327 arranged to direct the light out of the housing via protective window 328.

In the embodiment shown in figure 11, a white light filament source 325 is once again used. In this embodiment an internally reflecting light guide (such as a fibreoptic) is used. The fibreoptic may be connected to a light applicator to be connected to the skin as will be described hereafter.

25

The apparatus of figure 12 shows an applicator pad or patch structure 426 which is typically flexible in nature, permitting the pad 426 to be conformed to the shape of the body part to which it is applied. As shown in figures 13 to 15 additionally, light is directed to the pad or patch structure 426 by a flexible fibreoptic 435 which has a

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connector 436 arranged for mating connection to a corresponding connector 437 provided for the pad or patch structure. The pad or patch structure 426 has an imbedded fibreoptic arrangement 440 including a series of spaced lengths of fibreoptic 441 extending across the pad or patch structure.. In the embodiment shown in figure 13, the fibreoptic path lengths form a serpentine arrangement, although a number of paths connected in parallel would also provide a convenient and workable arrangement. As shown in figure 14 the fibreoptic 440 includes .a reflective surface cladding 442 surrounding a core 443. The surface cladding 442 ensures total internal reflection about the circumference of the fibreoptic except for an unclad window length 445 through which light can be emitted.

The pad or patch structure as shown in figures 12 to 15 provides a convenient arrangement in that light can be distributed widely over a large area of skin surface in a convenient and safe manner.

Particular benefits of the invention are the arrangement of the carrier and the photosensitive toxic material in discrete separate package portions, easily mixable at the required time in order to ensure that detrimental effects of early mixing or incorrect dosage ratios are avoided. The illumination apparatus configured to deliver non-laser light and/or configured to be placed against the target zone skin provide additional safety benefits and ensure that the skin is radiated to a consistent degree during treatment. This makes the kit particularly suitable for

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consumer/home use.



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## Claims:

1. A cosmetic kit for use in inhibiting hair growth, the  
5 kit comprising:
- a) a marker substance including a photosensitive  
toxic material to tag subcutaneous hair growth  
cells of a target zone of skin; and,
- 10 b) illumination apparatus for illuminating the skin  
in the target zone with light of a wavelength  
selected to effect preferential interaction with  
the hair growth cells tagged with the marker  
15 substance, resulting in a toxic effect  
inhibiting the hair growth capability of the  
tagged illuminated cells; wherein:
- (i) the marker substance is provided in a form  
20 comprising discrete portions of the  
photosensitive toxic material and a carrier  
material, the portions to be mixed prior to  
application to the target zone; and or,
- 25 (ii) the illumination apparatus includes an  
applicator configured to deliver non-laser  
light and/or configured to be placed  
against the target zone skin to deliver the  
illumination to the tagged hair growth  
30 cells.

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2. A cosmetic kit according to claim 1, wherein the portions of the photosensitive toxic material and the carrier material are dosed in a predetermined ratio.
- 5 3. A cosmetic kit according to claim 1 or claim 2, including a dispenser for dispensing the marker substance.
- 10 4. A cosmetic kit according to any preceding claim, including a container for the carrier material and or the photosensitive toxic material.
- 15 5. A cosmetic kit according to claim 4, wherein the container affords shielding of the photosensitive toxic material.
- 20 6. A cosmetic kit according to any preceding claim, wherein mixing means is provided for mixing the photosensitive toxic material and the carrier material.
- 25 7. A cosmetic kit according to claim 6, wherein the mixing means permits mixing of the photosensitive toxic material and the carrier material at a zone substantially sealed from the user.
- 30 8. A cosmetic kit according to any preceding claim, wherein a container for the photosensitive , toxic material and the carrier material comprises respective sealed zones containing the photosensitive toxic material and the carrier material respectively,

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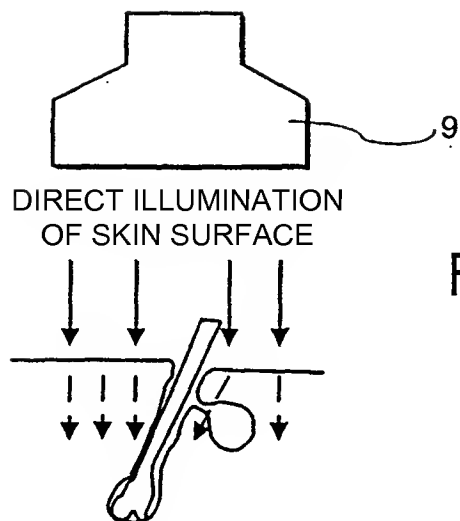
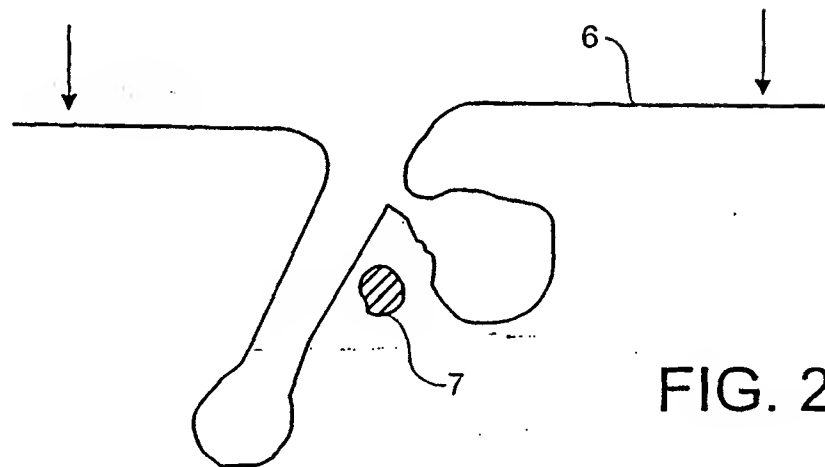
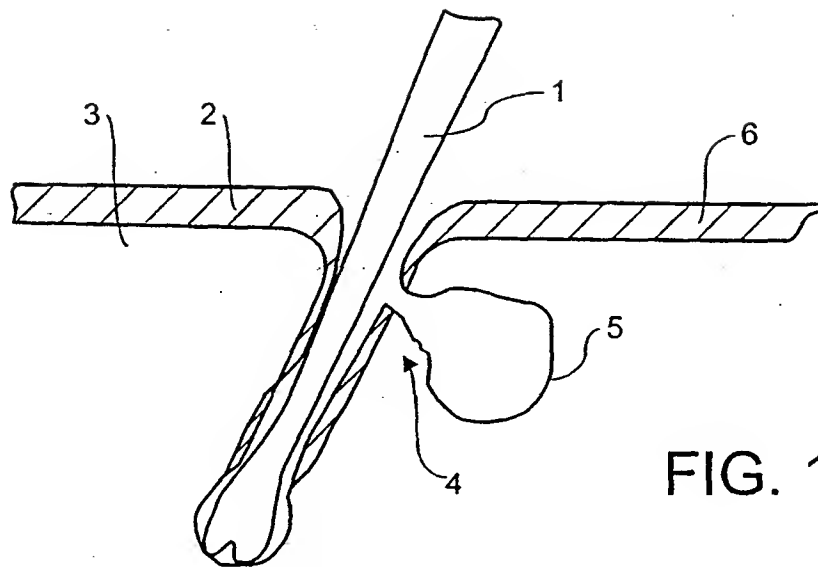
the zones being configured to be selectively breached or ruptured permitting mixing of the materials.

9. A cosmetic kit according to claim 8, wherein a mixing zone is provided adjacent the breachable sealed zones, the mixing zone communicating with a dispensing outlet.
10. A cosmetic kit according to any preceding claim,  
10 wherein the illumination apparatus includes window means surface arranged to overlay the target zone skin, the illumination being directed via the window means.
- 15 11. A cosmetic kit according to any preceding claim,  
wherein the illumination apparatus includes an illumination applicator having a flexible structure arranged to conform to the target zone skin body part.  
20
12. A cosmetic kit according to any preceding claim,  
wherein the apparatus includes:
  - 25 (a) an illumination applicator structure arranged to  
deliver illumination over a large area;
  - (b) a waveguide to connect with the illumination applicator; and,
  - 30 (c) a light source to direct light along the waveguide.

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13. A cosmetic kit according to any preceding claim, wherein the apparatus includes an illumination applicator structure having internal light reflecting walls and an associated light transmissive zone means through which reflected light is permitted to pass.
14. A cosmetic kit according to claim 13, wherein the applicator structure comprises one or more lengths of fibreoptic.
15. A cosmetic kit according to claim 13 or claim 14, wherein the applicator structure comprises a plurality of lengths of fibre optic, the lengths being arranged to deliver light at different zones of the applicator.

1/4



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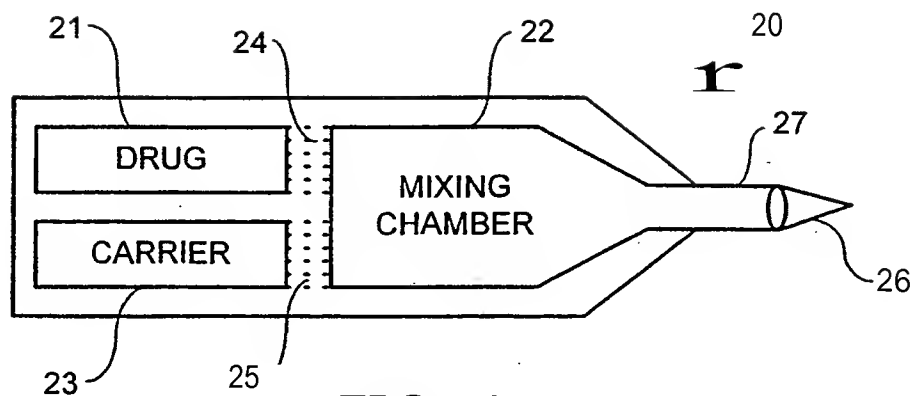


FIG. 4

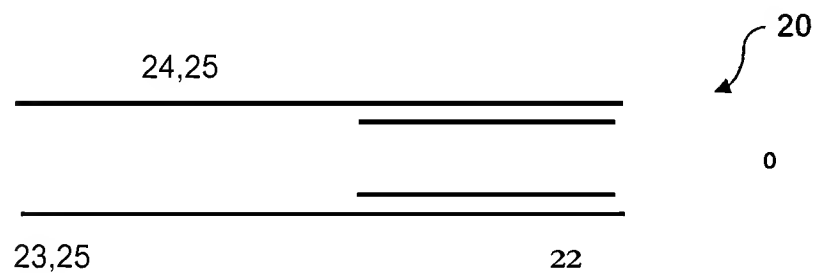


FIG. 5

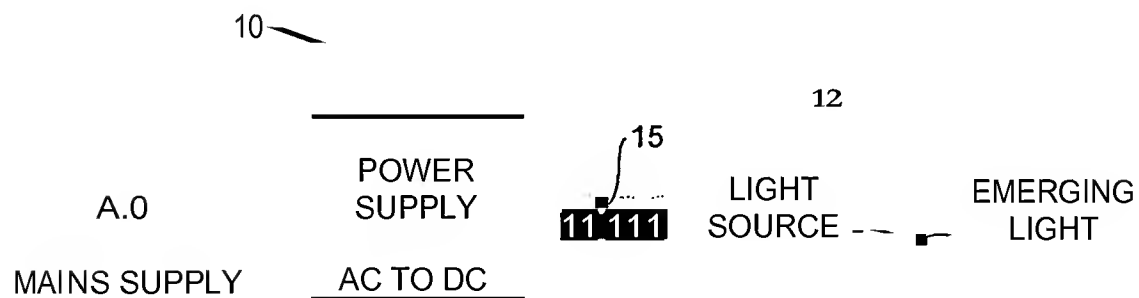


FIG. 6

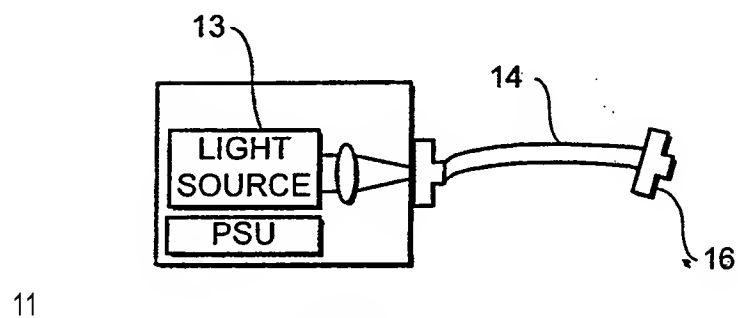
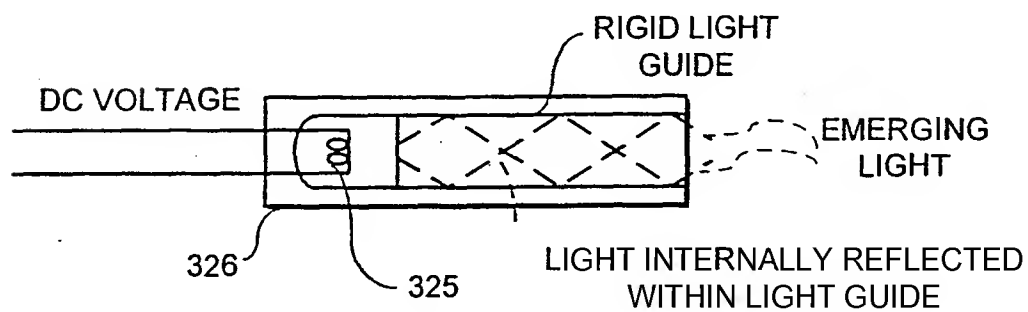
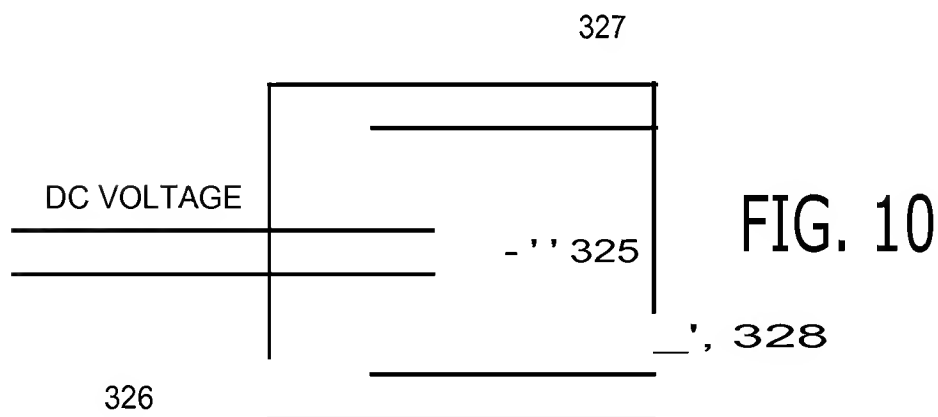
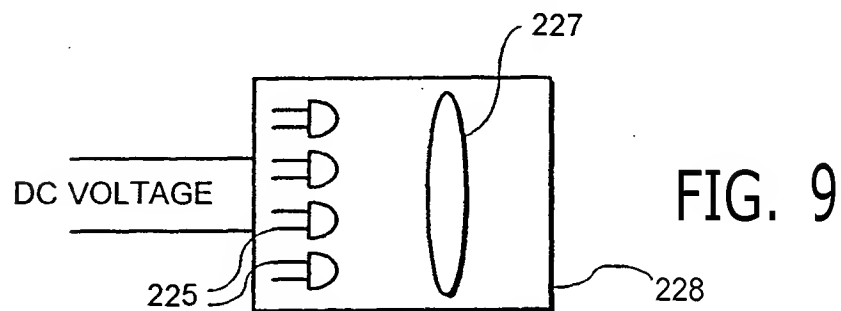
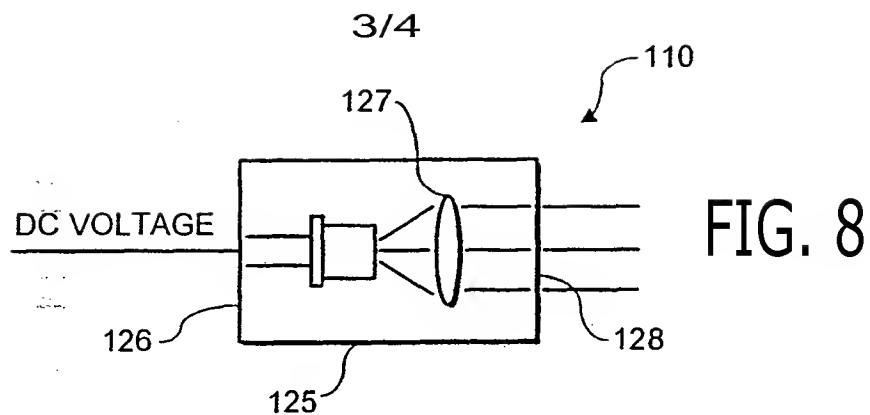
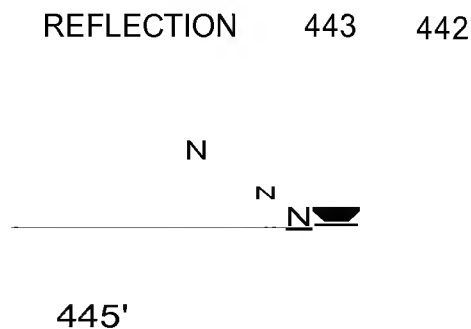
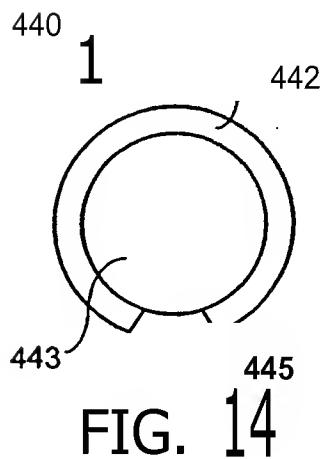
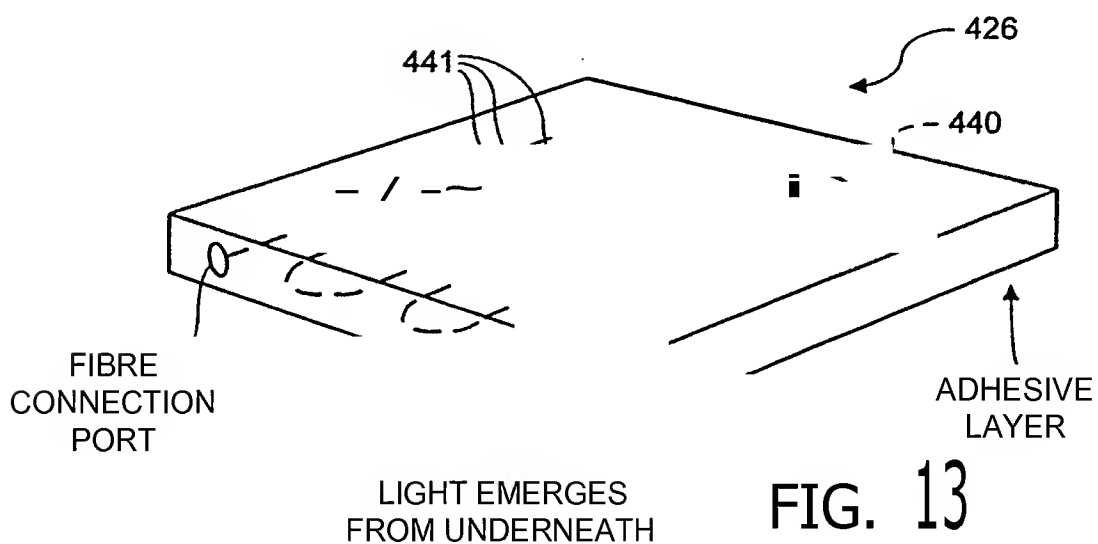
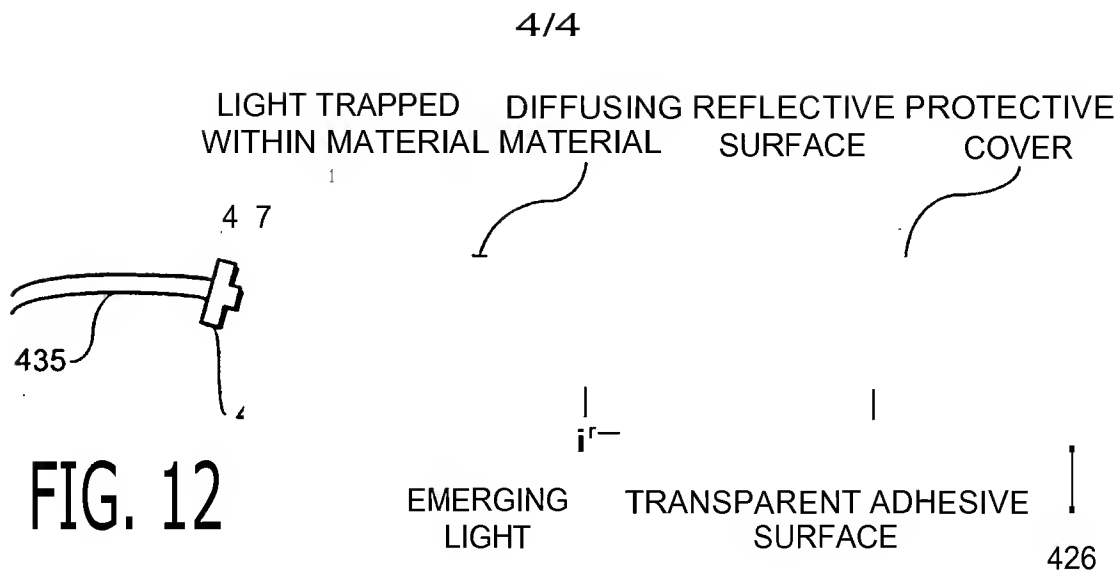


FIG. 7







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Documentation <b>searched</b> other than minimum <b>documentation</b> to the extent that such <b>documents</b> are included in the fields <b>searched</b>							
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Category °	Citation of document, with indication, <b>where appropriate</b> , of the <b>relevant passages</b>		Relevant to claim No.				
X	140 97! 32046! A! (NEW YORK! BLOOD! CENTER! INC) 4! September! 1997! (1997-09-04) page! 3, line! 13! -! line! 22 page! 4, line! 11! -! line! 28 page! 5, line! 3! -! line! 12		1-7, 10, 12				
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° Special categories of cited documents : <table border="0"> <tr> <td style="vertical-align: top;">           'A' document defining the general state of the art which is not considered to be of particular relevance            'E' earlier document but published on or after the international filing <b>date</b>            'L' document which <b>may throw doubts on priority</b> claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)            'O' document referring to an oral disclosure, use, exhibition or other means            "P" document published prior to the international filing date but later than the <b>priority</b> date claimed         </td> <td style="vertical-align: top;">           'I' later document published after the <b>international</b> filing date or <b>priority</b> date and not in conflict with the application but cited to understand the principle or theory underlying the invention            'X' document of particular relevance: the claimed invention cannot be considered novel or cannot <b>be considered</b> to involve an <b>inventive</b> step when the document is <b>taken alone</b>            'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.            document member of the same patent family         </td> </tr> </table>				'A' document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the international filing <b>date</b> 'L' document which <b>may throw doubts on priority</b> claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O' document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the <b>priority</b> date claimed	'I' later document published after the <b>international</b> filing date or <b>priority</b> date and not in conflict with the application but cited to understand the principle or theory underlying the invention 'X' document of particular relevance: the claimed invention cannot be considered novel or cannot <b>be considered</b> to involve an <b>inventive</b> step when the document is <b>taken alone</b> 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. document member of the same patent family		
'A' document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the international filing <b>date</b> 'L' document which <b>may throw doubts on priority</b> claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O' document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the <b>priority</b> date claimed	'I' later document published after the <b>international</b> filing date or <b>priority</b> date and not in conflict with the application but cited to understand the principle or theory underlying the invention 'X' document of particular relevance: the claimed invention cannot be considered novel or cannot <b>be considered</b> to involve an <b>inventive</b> step when the document is <b>taken alone</b> 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. document member of the same patent family						
.Date of the actual completion of the international search <b>19! September! 2000</b>		Date .4 mailing of the international search report <b>26/09/2000</b>					
Name and mailing address of the ISA <b>European</b> Patent Office. P.B. <b>5818</b> Patentlaan 2 NL -2280 HV Rijswijk Tel. (a31-70) <b>340-2040</b> , Tx. 31 651 epo nl. Fax: (+31-70) 340-3016		Authorized officer <b>P! etter r E</b>					

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US! 5! 669! 916! A! (ANDERSON! RICHARD! ROX) 23! September! 1997! (1997-09-23) cited! in! the! application column! 4, line 25! - line 42	1,2
X	US! 5! 474! 528! A! (MESEROL! PETER! M) 12! December! 1995! (1995-12-12) column! 6, line! 6! -column! 7, line! 9 column! 8,! line! 17! -column! 9,! line! 2	1-8, 10-12
Y	US! 4! 093! 067! A! (HOLLANDER! JR! EDWARD! F) 6! June! 1978! (1978-06-06) column! 2,! line! 54! -column! 3, line! 2	8,9
Y	WO! 99! 10046! A! (BIEL! MERRILL! A! ;ADVANCED PHOTODYNAMIC! TECHNOLO! (US)) 4! March! 1999! (1999-03-04) abstract	11
Y	US! 5! 849! 027! A! (CESATI! CLAUDIO ET! AL) 15! December! 1998! (1998-12-15) column! 4, line! 20! -! line! 32 column! 6, line! 2! -! line! 13	13-15
A	US! 3! 736! 933! A! (SZABO! B) 5! June! 1973! (1973-06-05) abstract	8,9
A	US! 5! 835! 648! A! (ANDERSON! STEVEN! C ET! AL) 10! November 1998! (1998-11-10) column! 3, line! 17! -! line! 59	13,14
A	US! 5! 519! 534! A! (COLE! JOHN ET! AL) 21! May! 1996! (1996-05-21) abstract	13

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9732046	A	<b>04-09-1997</b>	AU 2135997 A CA 2247611 A EP 0883695 A JP 2000506140 T	<b>16-09-1997</b> <b>04-09-1997</b> <b>16-12-1998</b> <b>23-05-2000</b>
<b>WO 9507077</b>	A	<b>16-03-1995</b>	AU 7543794 A	<b>27-03-1995</b>
<b>US 5669916</b>	A	23-09-1997	AU 689962 B AU 3685095 A CA 2201123 A EP 0783347 A JP 10506554 T WO 9609853 A US 5989267 A	<b>09-04-1998</b> <b>19-04-1996</b> <b>04-04-1996</b> <b>16-07-1997</b> <b>30-06-1998</b> <b>04-04-1996</b> <b>23-11-1999</b>
US 5474528	A	12-12-1995	WO 9704836 A	13-02-1997
<b>US 4093067</b>	A	<b>06-06-1978</b>	NONE	
<b>WO 9910046</b>	A	<b>04-03-1999</b>	AU 9294298 A EP 1009483 A	<b>16-03-1999</b> <b>21-06-2000</b>
US 5849027	A	15-12-1998	NONE	
US 3736933	A	05-06-1973	NONE	
US 5835648	A	<b>10-11-1998</b>	NONE	
US 5519534	A	<b>21-05-1996</b>	AU 2651795 A WO 9532441 A	18-12-1995 <b>30-11-1995</b>

